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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/768,511	01/30/2004	Oswaldo da Costa e Silva	16313-0280	9257

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EXAMINER	
COLLINS, CYNTHIA E	
ART UNIT	**PAPER NUMBER**
1638	

DATE MAILED: 02/03/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/768,511	SILVA ET AL.	
	Examiner	Art Unit	
	Cynthia Collins	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 January 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1,2,11,12* is/are allowed.

6)☒ Claim(s) *3-10,13-16,19 and 20* is/are rejected.

7)☒ Claim(s) *17 and 18* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 January 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *0104,0704*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Information Disclosure Statement

Initialed and dated copies of Applicant's IDS forms 1449, filed July 2, 2004 January 30, 2004, are attached to the instant Office action.

Several items of information in the IDS forms 1449 fail to comply with all the requirements of 37 CFR 1.97 and 37 CFR 1.98; these items were not considered, and a line has been drawn through the citations to show that they have not been considered. Each publication listed in an information disclosure statement must be identified by publisher, author (if any), title, relevant pages of the publication, date, and place of publication.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 3-10, 13-16 and 19-20 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The claims are drawn to transgenic plant cells plants and seed transformed by with a nucleic acid encoding a polypeptide whose expression increases the cell's tolerance to an environmental stress wherein the nucleic acid hybridizes to SEQ ID NO:5

or its complement under defined stringency conditions, or encodes a polypeptide having at least 90% sequence identity with SEQ ID NO:8. The claims are also drawn to the nucleic acid used for transformation, and methods of plant transformation.

The specification describes SEQ ID NO:5 (also designated CC-2) as a nucleic acid sequence obtained from *Physcomitrella patens* that encodes an amino acid sequence of SEQ ID NO:8 (pages 41-50; sequence listing). The specification also describes SEQ ID NO:8 as exhibiting 40-49% sequence identity and 54-61% sequence similarity to five different cell division control polypeptides obtained from *Arabidopsis thaliana*, *Mus musculus*, *Homo sapiens*, *Saccharomyces cerevisiae* and *Schizosaccharomyces pombe* (page 46 Table 3). The specification additionally describes transgenic *Arabidopsis* plants transformed with a construct comprising SEQ ID NO:5 operably linked to a promoter in a sense orientation, said transgenic plants having increased drought stress tolerance as compared to nontransgenic wild type plants (page 54 Table 7; Figure 4). The specification does not describe other isolated nucleic acids that hybridize under the recited stringency conditions to SEQ ID NO: 5, or that encode polypeptides having at least 90% sequence identity with SEQ ID NO:8.

The Federal Circuit has recently clarified the application of the written description requirement to coding sequences. The court stated that "A description of a genus of cDNAs may be achieved by means of recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus." See *University of California v. Eli Lilly and Co.*, 119 F.3d 1559, 1569; 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

In the instant case Applicant has not described a representative number of species falling within the scope of the claimed genus which encompasses numerous undisclosed and uncharacterized nucleic acids that hybridize under the recited stringency conditions to SEQ ID NO: 8 or that encode polypeptides having at least 90% sequence identity with SEQ ID NO:5, nor the structural features unique to the genus.

Claims 3-10, 13-16 and 19-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a nucleic acid of SEQ ID NO:5 or a nucleotide sequence encoding SEQ ID NO:8, and for transgenic plants and plant cells transformed with a construct comprising a nucleic acid of SEQ ID NO:5 or a nucleotide sequence encoding SEQ ID NO:8 operably linked to a promoter in a sense orientation, and methods of making said plants and cells, does not reasonably provide enablement for other nucleic acid sequences, or for transgenic plants or plant cells transformed with other nucleic acid sequences. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are drawn to transgenic plant cells plants and seed transformed by with a nucleic acid encoding a polypeptide whose expression increases the cell's tolerance to an environmental stress wherein the nucleic acid hybridizes to SEQ ID NO:5 or its complement under defined stringency conditions, or encodes a polypeptide having at least 90% sequence identity with SEQ ID NO:8. The claims are also drawn to the nucleic acid used for transformation, and methods of plant transformation.

The specification discloses the isolation from *Physcomitrella patens* of a nucleic acid of SEQ ID NO:5 (also designated CC-2) that encodes an amino acid sequence of SEQ ID NO:8 (pages 41-50; sequence listing). The specification also discloses that SEQ ID NO:8 exhibits 40-49% sequence identity and 54-61% sequence similarity to five different cell division control polypeptides obtained from *Arabidopsis thaliana*, *Mus musculus*, *Homo sapiens*, *Saccharomyces cerevisiae* and *Schizosaccharomyces pombe* (page 46 Table 3). The specification additionally discloses how to use a nucleic acid of SEQ ID NO:5 to make transgenic *Arabidopsis* plants by transforming *Arabidopsis* plants with a construct comprising SEQ ID NO:5 operably linked to a promoter in a sense orientation, said transgenic plants having increased drought stress tolerance as compared to nontransgenic wild type plants (page 54 Table 7; Figure 4).

The specification does not disclose other isolated nucleic acids that hybridize under stringent conditions to SEQ ID NO: 5, or that encode polypeptides having at least 90% sequence identity with SEQ ID NO:8 that can be used to increase the tolerance of a plant cell transformed therewith to drought or cold stress. The specification also does not disclose how to use SEQ ID NO:5 to increase tolerance to environmental stresses other than drought stress.

The full scope of the claimed invention is not enabled because the function of nucleic acid sequences that hybridize under stringent conditions to SEQ ID NO: 5 or that encode polypeptides having at least 90% sequence identity with SEQ ID NO:8 is unpredictable, since structurally homologous sequences are not always functionally homologous.

See, for example, Whisstock J.C. et al. (Prediction of protein function from protein sequence and structure. Q Rev Biophys. 2003 Aug;36(3):307-40. Review), who teach

> "... prediction of protein function from sequence and structure is a difficult problem, because homologous proteins often have different functions. Many methods of function prediction rely on identifying similarity in sequence and/or structure between a protein of unknown function and one or more well-understood proteins. Alternative methods include inferring conservation patterns in members of a functionally uncharacterized family for which many sequences and structures are known. However, these inferences are tenuous. Such methods provide reasonable guesses at function, but are far from foolproof." (Abstract)

Whisstock J.C. et al. also teach at page 309 that while the observation that similar sequences determine similar structures gives us general confidence in homology modeling, much less reliable is the widely held assumption that proteins with very similar sequences should by virtue of their very similar structures have similar functions. Whisstock J.C. et al. further teach at page 309 that to reason from sequence and structure to function is to step on much shakier ground, that while many families of proteins contain homologues with the same function, the assumption that homologues share function is less and less safe as the sequences progressively diverge, and that even closely related proteins can change function through divergence to a related function or by recruitment for as very different function in such cases the assignment of function on the basis of homology in the absence of direct experimental evidence will give the wrong answer.

Whisstock J.C. et al. additionally teach at page 310 that a protein need not even change sequence to change function, as numerous proteins exhibit multiple functions in different cellular environments such that even if detailed in vitro studies on isolated

proteins do identity a function we cannot be sure we know the molecules full repertoire of biological activities, and that nonhomologous proteins may conversely have similar functions.

Whisstock J.C. et al. further teach that while general hints based on protein sequence, structure, genomics and interaction patterns may be useful in guiding experimental investigations of protein function,

> "inferring protein function from knowledge of the function of a close homologue is like solving the clue of an American crossword puzzle. Finding the word that satisfies the definition may be difficult but the task in principle is straightforward. Working out the function of a protein from its sequence and structure is like solving the clue of a British crossword puzzle. It is by no means obvious which features of the definition are providing the real clues, as opposed to misleading ones. Also, for both types of puzzle and for the suggestion of a protein function, even if your answer appears to fit it may be wrong." (pages 311-312).

In the instant case the specification does not provide sufficient guidance with respect to which nucleic acid sequences that hybridize under stringent conditions to SEQ ID NO: 5 or that encode polypeptides having at least 90% sequence identity with SEQ ID NO:8 can be used to increase the tolerance of a plant cell transformed therewith to drought or cold stress. Absent such guidance one skilled in the art would have to test each of the myriad sequences encompassed by the claims for its effect on the tolerance of a plant cell transformed therewith to drought and cold stress in order to discriminate between those sequences that can increase plant stress tolerance and those that cannot. Such a trial and error approach to practicing the claimed invention would constitute undue experimentation.

Allowable Subject Matter

Claims 1-2 and 11-12 are allowed.

Claims 17-18 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Remarks

Claims 1-20 are deemed free of the prior art due to the failure of the prior art to teach or suggest an isolated nucleic acid of SEQ ID NO:5 or encoding SEQ ID NO:8 or an isolated nucleic acid that hybridizes to SEQ ID NO: 5 under the stringency conditions defined in the claims or an isolated nucleic acid that encodes a polypeptide having at least 90% sequence identity with SEQ ID NO:8.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia Collins whose telephone number is (571) 272-0794. The examiner can normally be reached on Monday-Friday 8:45 AM -5:15 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg can be reached on (571) 272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Cynthia Collins
Primary Examiner
Art Unit 1638

CC

Cynthia Collins

1/31/06